

## Probiotics in Clinical Practice: An Update

James P. Meschino, DC, MS

A review of the experimental and clinical studies pertaining to the health benefits of [probiotics](#) appeared in the journal *Nutrition Reviews* in July 2011.<sup>1</sup> Over the years, there have been many claims and theories about the health benefits of probiotics. The article by Taylor Wallace and fellow researchers is most helpful in bringing practitioners up to date as to the evidence-based use of probiotics, particularly with respect to their potential application in clinical practice. Let's review the clinically relevant points brought forward by Wallace, et al., as a means to help practitioners incorporate safe, responsible and effective probiotic recommendations into their daily practice.

### Probiotic Supplementation Benefits: An Overview

The human large intestine houses more than 1,000 different types of bacteria, known as microflora. Studies in recent years have shown that supplementation with health-promoting strains of bacteria can exert beneficial effects in terms of preventing certain ailments and helping to better manage others.

The health-promoting effects of gut-friendly bacteria are reported to include the following: immune bioregulation, improved digestion and absorption, vitamin synthesis (vitamin K, biotin and other B vitamins), inhibition of the growth of harmful bacteria and fungi, cholesterol reduction, and lowering of [gas distension](#). In fact, more than 700 randomized, controlled human studies provide strong evidence that probiotic supplementation may aid in preventing or treating various GI tract disorders, promoting GI health, and preventing metabolic syndrome.

For example, *Bifidobacteria* and *Lactobacilli* are commonly used probiotics in various supplements. Supplementation studies suggest that they may aid lactose digestion in lactose-intolerant individuals, reduce constipation and infantile diarrhea, assist resistance to infections, and reduce inflammatory conditions in the gut.

### Metabolic Effects of Probiotics and the Gut Microflora

### Common Probiotic Species

Probiotic terminology can be a bit confusing because the word *acidophilus* is often used as a general name for a group of probiotic bacteria commonly used in probiotic supplements. This common group of bacteria include:

- *Lactobacillus acidophilus*
- *Lactobacillus casei*
- *Lactobacillus delbrueckii* (subspecies *bulgaricus*)
- *Bifidobacterium* species
- *Streptococcus salivarius* (subspecies *thermophilus*)

More accurately, *Lactobacillus* (*acidophilus*, *casei* and *bulgaris*) are the common lactobacillus bacteria used in many probiotic supplements. *Bifidobacterium infantis*, *B. brevis* and *B. longum* are also common *Bifidobacteria* that reside in the human large intestine and vagina, and are also popular constituents of probiotic formulations.<sup>2</sup> *B. infantis* was shown to dramatically reduce irritable bowel syndrome (IBS) in a recent clinical trial.<sup>3</sup>

The lower number of *Bifidobacteria* in formula-fed babies has been linked to risk of diarrhea and allergies that are usually associated with babies who are not breast-fed. As well, *Bifidobacteria* produce lactic acid instead of gas (like *E. coli*), and thus, infants and adults with more *Bifidobacteria* have been shown to have less gas and digestive problems. There is also a significant difference in the incidence of antibiotic-associated diarrhea in children receiving probiotic-supplemented (enriched with *Bifidobacterium*) formula (16 percent) than non-supplemented formula (31 percent).<sup>4</sup>

Bacteria within the gut microflora degrade and/or ferment various substrates including starches, soluble dietary fibers, and other carbohydrate sources available in lower concentrations (oligosaccharides and portions of non-absorbable sugars and sugar alcohols). Proteins and amino acids can be effective growth substrates for colonic bacteria. The same is true for bacterial secretions, lysis products, sloughed epithelial cells, and mucins.

A wide range of bacterial enzymes degrade these materials into various intermediates, which are then fermented into organic acids, histamine, carbon dioxide, and other neutral, acidic, and basic end products. The intermediate and end products formed in this process have been shown to provide various health influences of importance:

**Suppress Growth of Harmful Bacteria and Other Undesirable Microorganisms:** Acidification of the large bowel by probiotics may inhibit the growth of pathogens and the production of toxic compounds such as ammonia and amines. Probiotics can compete for some of the same attachment sites as harmful bacteria and fungi, use the same nutrients, and produce antimicrobial compounds that inhibit the growth of these pathogens. Many probiotics are known to inhibit adhesion and

displace pathogens, such as *Salmonella*, *Escherichia coli* and *Listeria*.

*Cancer Inhibition:* Carbohydrate fermentation yields short-chain fatty acids such as butyrate, which inhibit DNA synthesis and stimulate apoptosis (programmed cell death).

*Enhanced Nutrient Absorption:* Carbohydrate fermentation and short-chain fatty acids improve the absorption of calcium, magnesium and phosphorus.

*Immune Modulation:* Various probiotics have been shown to modulate the [immune system](#). In short, various bacterial components and secretions modulate the activity of gut immune cells (dendritic cells, macrophages) via stimulation of signal transduction pathways within various immune cells. In turn, this effect has been shown to enhance immune system efficiency at both the mucosal and systemic levels. As such, probiotic supplementation has the potential to improve the body's global immune function, in addition to local gut immunity. Bacterial components and secretions have also been shown to up-regulate the release of immune-modulating cytokines and chemokines from intestinal epithelial cells. Intestinal epithelial cells play an active role in the innate immune response.

Some probiotics have also been shown to alter mucosal immune function via enhancement of antibody production, and increase of phagocyte and natural killer-cell activity, as well as the induction of regulatory dendritic cells and various T-lymphocytes. Some probiotic bacteria, particularly *Bifidobacteria*, also encourage the maturation of dendritic cells. Like macrophages, dendritic cells are both phagocytic (destroying invaders) and primary antigen-presenting cells, which recruit other immune cells into the fight against pathogens.

*Improve Digestion:* Friendly gut bacteria also produce digestive enzymes, improving digestion in individuals with various food intolerances (e.g., lactose intolerance).

*Guard Against Antibiotic-Associated Diarrhea and Related Complications:* Probiotic supplementation has been shown to restore normal gut function and microflora activity following antibiotic therapy.

*Reduce Risk of Intestinal Infections:* Gut microbiota is reported to contribute to human protein homeostasis. Germ-free animals are highly susceptible to infections, providing evidence that the intestinal microbiota is considered an important defense barrier.

*Decrease Inflammation:* Probiotics have been shown to down-regulate the activity of nuclear factor-kappa beta (NF-kb) within intestinal epithelial cells. [NF-kb](#) is a transcription factor that promotes the release of many inflammatory cytokines, which can have a local or systemic effect on various inflammatory conditions. As such, inhibiting the activity of NF-kb is thought to be a key mechanism through which probiotic supplementation may be an important adjunct in the management of inflammatory bowel disease, as well as rheumatoid arthritis, other autoimmune diseases, asthma, psoriasis and sepsis. Probiotic supplementation has also been shown to increase release of interleukin 10 (IL-10), an important anti-inflammatory cytokine, from dendritic cells.

*Improved Intestinal Barrier :* Probiotics also enhance epithelial barrier function through several mechanisms, including effects on epithelial tight junction proteins, increased production of intestinal mucus, enhanced mucosal immunoglobulin A responses, and other mechanisms. Animal studies suggest that a specific probiotic combination can normalize intestinal barrier function in colitis.

Clinical Applications and Considerations

Research over the past 25 years suggests that probiotic supplements may be a useful adjunct in the management of various health conditions such as antibiotic-associated diarrhea, necrotizing enterocolitis, inflammatory bowel disease, and extraintestinal disorders including atopic dermatitis and recurrent urinary tract infections. Other considerations include rheumatoid arthritis, other autoimmune diseases, immune-compromised states, psoriasis, food intolerances, and other conditions in which digestion may be compromised. Probiotic supplementation may also be a consideration as part of a colon cancer prevention program.

At present, there is no single probiotic combination considered to be the gold standard by the scientific community. To view a summary of the recent studies on the effects of probiotics on systemic and mucosal immune function, barrier function and metabolism, refer to Table 1 (pages 396-7) in the paper by Wallace TC, et al., in *Nutrition Review* (complete reference provided at the end of this article). Researchers in this field suggest using the probiotic bacteria that have been shown to provide the desired health outcome on a case-by-case basis. The health outcomes provided by each strain of bacteria are shown in Table 1, as mentioned above.

Having looked at this information, I suggest using a probiotic supplement that contains various strains of bacteria, ensuring the presence of *Bifidobacteria* and *Lactobacilli*. For example, the probiotic combination supplement shown to improve intestinal barrier function in animals with colitis included *Lactobacillus casei*, *Lactobacillus plantarum*, *Lactobacillus acidophilus*, *Lactobacillus delbrueckii* (subspecies *bulgaricus*), *Bifidobacterium longum*, *Bifidobacterium breve*, *Bifidobacterium infantis* and *Streptococcus salivarius* (subspecies *thermophilus*).

Note that a specific dosage of probiotic supplementation has yet to be standardized; thus, as practitioners we are left at the mercy of the product manufacturers and the dosage recommendations listed on the label of the various products. However, probiotic supplementation has been shown to be superior to deriving probiotics from functional foods (e.g., yogurt). Supplementation has been shown to be a more consistent method of ensuring probiotic intake and provides a much higher dose. However, probiotic-containing foods can add some additional benefit in this regard.

From a safety standpoint, probiotics should be used with caution in children, elderly persons and individuals with major risk factors or multiple minor risk factors.

Remember that supplementation with *prebiotics* such as fructo-oligosaccharide (FOS) and inulin can also help spur the growth of friendly gut bacteria. Prebiotics are the food upon which friendly bacteria thrive. Many health outcomes available from probiotic supplementation have also been shown to occur with supplementation of prebiotics. Thus, daily ingestion with soluble fiber, as well as 1,000-5,000 mg of **FOS and inulin**, may be helpful in the prevention and management of some of the health conditions mentioned above. As well, it seems to make sense to take a prebiotic supplement in conjunction with probiotics to optimize the potential for probiotic bacteria to thrive in the large bowel.

## References

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